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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,189	10/31/2003	Robert G. Aslanian	AL01348K18	3527

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
2000 GALLOPING HILL ROAD
KENILWORTH, NJ 07033-0530

EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,189	ASLANIAN ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-25,46,51,52 and 55-57* is/are pending in the application.

4a) Of the above claim(s) *2-25 and 56-575* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46,51,52 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of group II with the bispyridinyl bispiperidine compound of claim 51 in the reply filed on Sept. 22,2006 is acknowledged.

Claims 1, 26-45, 47-50, 53-54, 58-61 have been canceled. Claims 2-25, 46, 51-52, 55-57 are pending.

Applicants' attention is drawn to that the currently amended claims and the election are inconsistent. Please note that the election was made without traverse to the combination composition and method of using for the bispyridinyl bispiperidine compounds of claim 51 and loratadine/desloratadine. Yet, the non-elected compounds have not been canceled from the claims. Further, in applicants' remark, it was stated that claim 59 has been amended, yet no amended claim was presented but claim 59 was canceled. Based on the election, claims 46, 51, 52 and 55 wherein the combination composition and method of a compound selected from claim 51 bispyridinyl bispiperidine and one H1 receptor antagonist selected from loratadine or desloratadine is examined. The remaining subject matter and claims 2-25, 56-57 are withdrawn from consideration as being drawn to the non-elected invention per 37 CFR 1.142(b).

2. Claims 46, 51, 52, 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

A survey of the specification was made. On pages 1, 11-12 and 129, a combination of histamine H1 receptor antagonist and at least one histamine H3 receptor antagonist to be used together was described. However, a *single composition* containing a single compound among those of claim 51 with either loratadine or desloratadine was not found. While general description support the concept of combination use of compounds of formula I and at least one histamine H3 receptor antagonist, does not offer any description of the dosage, carrier etc. for a specific compound and a specific H3 antagonist. As set forth by the court in Perdue Pharm. V. Faulding Inc. 56 USPQ2d 1481, "...one cannot disclose a forest in the original application and

then later pick a tree out of the forest and say here is my invention...". There is no antecedent basis for a *single composition* with two specific active ingredients.

3. Claims 46, 51, 52, 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claims are drawn to combination composition of a histamine H1 receptor antagonist of claim 51 and at least one histamine H3 receptor antagonist of loratadine or desloratadine and method of using such.

The state of the art and predictability

Combination of pharmaceutical active ingredients is highly unpredictable art. As evidence by the prior art recited on page 1 of the specification US 5,869,479, It was clearly documented that, only specific H3 active compounds can be combined with specific H1 active compounds (see col. 3, lines 17-35) and screening must be conducted to pick and choose such compounds together with suitable clinical trials (see col. 4 lines 11-14). A pre-requisite of the H3 antagonist to have a Ki values less than 200 nM in a Korte et al. testing was explicitly required (see col. 3 line 33-35).

The amount of guidance and working examples

As it was discussed supra that while general description for combination use of a histamine H1 receptor antagonist and at least one histamine H3 receptor antagonist, no specific single combination of composition was described (see section 2). Further, the specification provided no information as to what procedure was employed for the Ki measurement, nor any Ki value for any specific compound (see p.129). While mere recitation of range in a screening test can verify utility of the broadly encompassed compounds, no information for picking and choosing a particular compound for specific combination of a single combined dose formulation. Further, no clinical trial of any combination was disclosed. The claimed compounds are new (see parent patent US 6,720,328 claims 26-29, 31-32) and no information on the specific Ki or how to form a single dosage unit with loratadine or desloratadine can be found in the specification.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 46, 51, 52, 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreutner et al. US 5,869,479.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kreutner et al. '479 disclosed combination composition of loratadine or desloratadine with H3 antagonist (see col. 6-7, example 6-7) and showed that enhanced decongestion was obtained.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the Kreutner et al. composition is that instead of H3 antagonist thioperamide, the instant claims employed the new compounds of claim 51. Generically, Kreutner et al. provided procedure of screening test and parameters for picking and choosing other H3 receptor antagonist wherein a 200nM Ki was required (see col. 6 lines 43-45).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to conduct the testing procedure for other H3 receptor antagonist knowing that such H3 receptor antagonist may qualify as an alternative choice of combination component in the Kreutner et al. combination wherein synergism was observed.

5. Claims 46, 51, 52, 55 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6-8 of US Patent No. 5,869,479 in view of US 2004,0198743.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kreutner et al. '479 claimed combination composition of loratadine or desloratadine with H3 antagonist (see col. 6-7, example 6-7) and showed that enhanced decongestion was obtained.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the Kreutner et al. composition is that instead of H3 antagonist thioperamide, the instant claims employed the new compounds of claim 51. Generically, Kreutner et al. provided procedure of screening test and parameters for picking and choosing other H3 receptor antagonist wherein a 200nM Ki was required (see col. 6 lines 43-45). Hey et al. '743 further provided evidence that analogous pyrimidinyl bispiperidines of claim 51 and thioperamide (see Hey '743 claim 1 and 6) are alternative choices for such composition and method under the 200 nM Ki guidelines.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to conduct the testing procedure for other H3 receptor antagonist knowing that such H3 receptor antagonist may qualify as an alternative choice of combination component in the Kreutner et al. combination wherein synergism was observed. Especially, analogous compounds of the claims have been evidence to be optional choices with analogous activity (see Hey '743 claim 1 and 6).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Nov. 28, 2006

Celia Chang
Primary Examiner
Art Unit 1625